426 Rec'd PCI/PIO 2 8 DEC 2000

FORM I	PTO-139	00 (Modified) U.S. DEPARTMENT	OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER		
TRANSMITTAL LETTER TO THE UNITED STATES			K0208.014			
		DESIGNATED/ELECTE	U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 1.5)			
CONCERNING A FILING UNDER 35 U.S.C. 371				09/720762		
INTE		TONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED		
TITLI		PCT/JP99/03459 NVENTION	29 June 1999	29 June 1998		
1			GE AND PRE-FILLED SYRINGE			
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		T(S) FOR DO/EO/US				
YAN	IASE	L, Kazuyuki, et al.				
Appli	cont 1		ates Designated/Elected Office (DO/EO/US)	C. C. 11 Van Van and other information.		
1.	X		items concerning a filing under 35 U.S.C. 371			
2.			QUENT submission of items concerning a file	<u> </u>		
3.	X	examination until the expiration	gin national examination procedures (35 U.S. n of the applicable time limit set in 35 U.S.C.	C. 371(1)) at any time rather than delay 371(b) and PCT Articles 22 and 39(1).		
4.		A proper Demand for Internation	nal Preliminary Examination was made by the	e 19th month from the earliest claimed priority date.		
5.	X		lication as filed (35 U.S.C. 371 (c) (2))			
			r (required only if not transmitted by the International Control of the In	rnational Bureau).		
	b.  has been transmitted by the International Bureau					
		<del>-</del>	application was filed in the United States Rec	· ,		
6. 7	X	A translation of the International Application into English (35 U.S C. 371(c)(2)).				
7. °	×	A copy of the International Search Report (PCT/ISA/210).				
8.		Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))				
•		a.  are transmitted herewith (required only if not transmitted by the International Bureau).				
],		<ul> <li>b.   have been transmitted by the International Bureau.</li> <li>c.   have not been made; however, the time limit for making such amendments has NOT expired.</li> </ul>				
		<ul> <li>c.  have not been made; however, the time limit for making such amendments has NOT expired.</li> <li>d.  have not been made and will not be made.</li> </ul>				
9.		A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).				
10.	X	An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).				
11.	X	r,				
12.		,				
I	tems :	13 to 18 below concern documen	at(s) or information included:	!		
13.	· ·					
14.	X	An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.				
15.	X					
j		A SECOND or SUBSEQUENT	f preliminary amendment.			
16.		☐ A substitute specification.				
17.		A change of power of attorney and/or address letter.				
18.	X	Certificate of Mailing by Express Mail				
19.	X	Other items or information:	· · · · · · · · · · · · · · · · · · ·			
		International Preliminary Exa PTO-1449	imination Report			
		PTO-1449 PCT/RO/101				
		PCT/IB/301				
		PCT/IB/304 PCT/IB/308				
		PCT/IB/332				
		PCT/306 (mailed on Jan. 12, J	- · · · · · · · · · · · · · · · · · · ·			
	Notification of Change of Applicant filed on August 11, 2000					

8 Rec'd PCT/PTO 28 DEC U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 1.5) INTERNATIONAL APPLICATION NO. ATTORNEY'S DOCKET NUMBER PCT/JP99/03459 K0208.014 20. The following fees are submitted: CALCULATIONS PTO USE ONLY BASIC NATIONAL FEE ( 37 CFR 1.492 (a) (1) - (5)) : ☐ Search Report has been prepared by the EPO or JPO . . . . . . . . . \$930.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) \$720.00 No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) . . . . . \$790.00 Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2) paid to USPTO ..... \$1,070.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4)..... \$98.00 ENTER APPROPRIATE BASIC FEE AMOUNT = \$910.00 Surcharge of \$130.00 for furnishing the oath or declaration later than months from the earliest claimed priority date (37 CFR 1.492 (e)). \$0.00 **CLAIMS** NUMBER FILED NUMBER EXTRA **RATE** Total claims 0 X \$0.00 - 20 = 0 \$0.00 - 3 = х Independent claims Multiple Dependent Claims (check if applicable). \$270.00 TOTAL OF ABOVE CALCULATIONS \$1,180.00 Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement most also be filed (Note 37 CFR 1.9, 1.27, 1.28) (check if applicable). \$0.00 **SUBTOTAL** \$1,180.00 Processing fee of \$130.00 for furnishing the English translation later than □ 20 months from the earliest claimed priority date (37 CFR 1.492 (f)). \$0.00 TOTAL NATIONAL FEE = \$1,180.00 Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be appropriate cover sheet (37 CFR 3.28, 3.31) (check if applicable). X \$40.00 TOTAL FEES ENCLOSED \$1,220.00 Amount to be: refunded N charged \$ X A check in the amount of \$1,220.00 to cover the above fees is enclosed. Please charge my Deposit Account No. in the amount of to cover the above fees. A duplicate copy of this sheet is enclosed. The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment X to Deposit Account No. 16-0633 A duplicate copy of this sheet is enclosed. NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status. SEND ALL CORRESPONDENCE TO: Customer No. 23723 Benjamin Levi NAME 37,517 REGISTRATION NUMBER December 28, 2000 DATE

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ATTORNEY DKT NO.: K0208.014 PATENT

#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

YANASE, Kazuyuki, et al.

Group Art Unit: Not Yet Known

International Filing Date:

29 June 1999

Priority Date:

29 June 1998

International Application No.:

PCT/JP99/03459

U.S. Serial No.:

Not Yet Assigned

Examiner: Not Yet Known

U.S. Filing Date:

Herewith

For:

GASKET FOR PRE-FILLED SYRINGE AND PRE-FILLED SYRINGE

Honorable Commissioner of Patents & Trademarks

Washington, D.C. 20231

December 28, 2000

**BOX PCT APPLICATION** 

#### PRELIMINARY AMENDMENT

Sir:

Please amend the above-identified application as follows:

#### **IN THE CLAIMS**

1. A gasket [used] for a pre-filled syringe into which liquid is charged, wherein a peripheral side surface of the gasket that is in contact with an inner surface of the syringe barrel is provided with a restriction, and a periphery of a bottom surface of the gasket that is not in contact with the liquid is formed into a tapered shape.

- 2. The [A] gasket according to claim 1, wherein hardness of the gasket is 55 to 60 when the hardness is measured by a JIS hardness meter.
- 3. The [A] gasket according to claim 1, wherein one or both of the peripheral side surface that is in contact with an inner surface of the syringe barrel and [/or] a bottom surface that is in contact with liquid is laminated with polyethylene fluoride resin.
- 4. The [A] pre-filled syringe into which liquid is charged and tightly closed with the gasket described in [any one of] claims 1. 2 or [to] 3.
  - 5. The [A] pre-filled syringe according to claim 4, wherein the liquid is contrast medium.

#### **REMARKS**

The above-identified application has been amended with this national stage filing to conform the claims to U.S. practice. No new matter is presented.

In view of the present amendments, Applicants believe the present application is in condition for allowance and such action is respectfully requested.

Respectfully submitted,

Dated: December 28,2 188

Benjamin/Levi

Registration. No. 37,517 Attorney for Applicants

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#### SPECIFICATION

Gasket for Pre-Filled Syringe and Pre-Filled Syringe

#### Field of the Invention

The present invention relates to a gasket for a pre-filled syringe and the pre-filled syringe.

#### **Background Art**

In generally, chemical liquid is charged into a syringe barrel when it is used. In recent years, a pre-filled syringe in which chemical liquid is previously charged into the syringe barrel has been developed, and working load in medical site is reduced. Recently, a pre-filled syringe in which contrast medium is charged into the syringe is also Since the contrast medium has relatively high viscosity, it is considered that it is important to increase sliding ability of a gasket so as to reduce the charging pressure. Especially when a syringe barrel is made of polymeric resin, since the sliding ability of the gasket is inferior, silicon oil is applied onto a peripheral side surface of a gasket that is in contact with an inner surface of the syringe barrel to enhance the sliding ability, or polyethylene fluoride resin such as Teflon (registered trade name) is laminated. However, if silicon applied to a gasket is mixed into chemical liquid, it becomes foreign matter, this may cause product defect, and there is apprehension that such foreign matter may have toxicity to human body.

It is normal that the pre-filled syringe is sterilized after chemical liquid is charged or chemical liquid is charged in axenic conditions. Sterilization after charging is carried by heating the pre-filled syringe for example, but it is important to form the gasket into such a shape that high pressure chemical liquid caused by heat at the time of sterilization is not leaked. When polyethylene fluoride resin or the like is laminated on a gasket, since the polyethylene fluoride resin is hard, if the gasket is inserted into the syringe barrel, fine wrinkles may be generated on a peripheral side surface of the gasket, and chemical liquid may be leaked through the wrinkles at the time of sterilization.

The present inventor studies hard to solve these problems and as a result, the inventor invented the following inventions.

#### Summary of the Invention

According to claim 1, there is provided a gasket used for a prefilled syringe into which liquid is charged, wherein a peripheral side surface of the gasket that is in contact with an inner surface of the syringe barrel is provided with a restriction, and a periphery of a bottom surface of the gasket that is not in contact with the liquid is formed into a tapered shape.

In this gasket of claim 1, as described in claim 2, it is preferable that hardness of the gasket is 55 to 60 when the hardness is measured by a JIS hardness meter. Further, as described in claim 3, it is preferable that the peripheral side surface that is in contact with the inner surface of the syringe barrel and/or a bottom surface that is in contact with liquid is laminated with polyethylene fluoride resin.

According to claim 4, there is provided a pre-filled syringe into which liquid is charged and tightly closed with the gasket described in any one of claims 1 to 3.

In this pre-filled syringe of claim 4, the liquid is, for example,

contrast medium as described in claim 5.

In the gasket of claims 1 to 3 and the pre-filled syringe of claims 4 and 5, the gasket plays a role as a lid for tightly closing the liquid charged into the syringe barrel, and also plays a role as a piston when the pre-filled syringe is used. As the JIS hardness meter for measuring the hardness of the gasket, "Durometer" produced by Shimazu Seisakusho can be used for example. A preferable range of the hardness of the gasket measured by the JIS hardness meter is 57 to 59. Material of the gasket is not limited only if it has appropriate hardness, but usually, the material is normal butyl rubber, silicon rubber or polymeric resin, and more preferably, chlorinated butyle rubber.

The peripheral side surface that is in contact with the syringe barrel or the bottom surface that is in contact with liquid can be laminated with polyethylene fluoride resin using a conventionally known laminating method. Silicon may be applied to the peripheral side surface of the gasket that is in contact with the inner surface of the syringe barrel, but it is preferable that silicon is not applied to the bottom syringe that is in contact with the liquid charged into the syringe barrel. The silicon can also be applied by a conventionally known application method.

Material of the syringe barrel is not limited, and any of glass and resin can be used. Especially, resin is preferable, and example of the material is annular polyolefin fiber.

Liquid to be charged into the syringe barrel is not limited to the contrast medium, and liquid other than the contrast medium may be used. Example of contrast medium is iomeprole. An amount of liquid to be charged into the syringe barrel is usually about 10 to 200 ml, and

more preferably 50 to 100 ml.

#### Brief Description of the Drawings

Fig.1 is a sectional view of a pre-filled syringe according to an embodiment of the present invention; and

Fig.2 is a side view of a gasket according to the embodiment of the invention.

#### Detailed Description of the Preferred Embodiments

A preferred embodiment of the present invention will be explained with reference to the accompanying drawings below.

As shown in Fig.1, in a pre-filled syringe 1 of this embodiment, a contrast medium 3 as one example of chemical liquid is charged in a cylindrical syringe barrel 2. The syringe barrel 2 is made of annular polyolefin fiber for example. The syringe barrel 2 is provided at its tip end (left end of the syringe barrel 2 in Fig.1) with a nozzle 4. The nozzle 4 is formed with a lure lock 5, and by mounting a cap 6 on the lure lock 5, the nozzle 4 is tightly closed. A columnar gasket 7 is inserted into the syringe barrel 2 from an opened rear end (right end of the syringe barrel 2 in Fig.1) of the syringe barrel 2, and the contrast medium 3 in the syringe barrel 2 is tightly closed by the gasket 7.

The gasket 7 is made of chlorinated butyle rubber for example, and the gasket 7 preferably has hardness of 55 to 60 degrees, more preferably 57 to 59 degrees when the hardness is measured using JIS hardness meter. As shown in Fig.2, a peripheral side surface 7a of the gasket 7 that is in contact with an inner surface of the syringe barrel 2 is formed with an annular restriction 8. A depth a of the restriction 8 is

about 0.05 to 1.0 mm, and more preferably, 0.1 to 0.5 mm if the gasket has a diameter b of 30 to 35 mm and a height c of 15 to 18 mm.

A bottom surface 7b (lower surface of the gasket 7 in Fig.2) that is in contact with the contrast medium 3 charged into the syringe barrel 2 is formed into a conical surface. The bottom surface 7b and the peripheral side surface 7a are laminated with polyethylene fluoride resin.

A central portion of a bottom surface 7c (upper surface of the gasket 7 in Fig.2) that is not in contact with the contrast medium 3 charged into the syringe barrel 2 is formed, as shown in Fig.2, with a threaded hole 9 into which a rod is fitted. As shown in Fig.2, a periphery of the bottom surface 7c is formed into a tapered slant 10. A range (range of the gasket 7 from an outer diameter in its diametrical direction) d where the slant 10 is formed is about 0.5 to 5 mm, and more preferably about 1 to 3 mm if the gasket has a diameter b of 30 to 35 mm and a height c of 15 to 18 mm.

According to this pre-filled syringe 1 having the above-described structure, the cap 6 is removed from the nozzle 4, and a tip end of an extension tube (not shown) for example is threadedly fitted to the lure lock 5. A rod (not shown) is fitted to the bottom surface 7c of the gasket 7. Then, the rod is pushed to push out the contrast medium 3 in the syringe barrel 2 through the extension tube, thereby charging the contrast medium 3 into a target position.

#### **Industrial Applicability**

According to the inventions of claims 1 to 5, the sliding ability when polyolefin resin is used as material of a syringe barrel is used is remarkably enhanced, and liquid is not leaked almost at all when the pre-filled syringe is sterilized. The gasket can smoothly move at the time of sterilization even when the gasket is pushed out, and there is no adverse possibility that the gasket is diagonally inclined with respect to a center axis of the syringe barrel.

#### WHAT IS CLAIMED IS:

- 1. A gasket used for a pre-filled syringe into which liquid is charged, wherein a peripheral side surface of the gasket that is in contact with an inner surface of the syringe barrel is provided with a restriction, and a periphery of a bottom surface of the gasket that is not in contact with the liquid is formed into a tapered shape.
- 2. A gasket according to claim 1, wherein hardness of the gasket is 55 to 60 when the hardness is measured by a JIS hardness meter.
- 3. A gasket according to claim 1, wherein the peripheral side surface that is in contact with an inner surface of the syringe barrel and/or a bottom surface that is in contact with liquid is laminated with polyethylene fluoride resin.
- 4. A pre-filled syringe into which liquid is charged and tightly closed with the gasket described in any one of claims 1 to 3.
- 5. A pre-filled syringe according to claim 4, wherein the liquid is contrast medium.

#### DESCRIPTION OF CHARACTERS

1 pre-filled	syringe
--------------	---------

- 2 syringe barrel
- 3 contrast medium
- 4 nozzle
- 5 lure lock
- 6 сар
- 7 gasket
- 7a peripheral side surface
- 7b ,7c bottom surface
- 8 annular restriction
- 9 threaded hole
- 10 tapered slant

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#### ABSTRACT OF THE DISCLOSURE

A gasket 7 used for a pre-filled syringe 1 into which liquid 3 is charged, wherein a peripheral side surface of the gasket 7 that is in contact with an inner surface of the syringe barrel 2 is provided with a restriction 8, and a periphery of a bottom surface 7c of the gasket 7 that is not in contact with the liquid 3 is formed into a tapered shape.

FIG.1

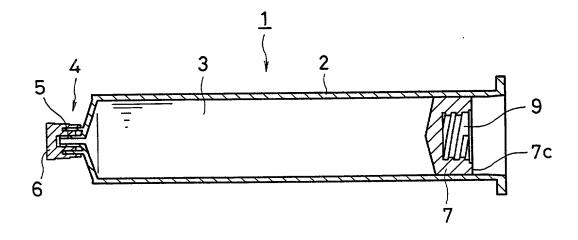
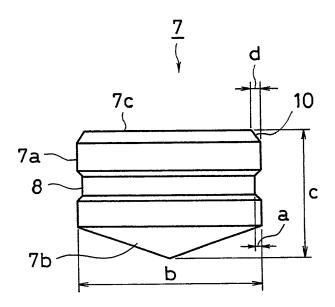


FIG.2



## COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

(Includes Reference to PCT International Applications)

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Gasket for Pre-Filled Syringe and Pre-Filled Syringe

tne specification	in of which (check only one item below):	
	is attached hereto.	
□1	was filed as United States application	
	Serial Noon	
	and was amended on (if applicable).	
⊠2	was filed as PCT international application	
	Number PCT/JP99/03459. on June 29, 1999	
	and was amended under PCT Article 19	
	on (if applicable).	

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56 (a).

## COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

(Includes Reference to PCT International Applications)

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

COUNTRY (if PCT, indicate "PCT"	APPLICATION NUMBER	DATE OF FILING (day, month, year)		TY CLAIMED 35 USC 119
Japan	JP-10-183005	June 29,1998	⊠5 YES	□6 NO
PCT	PCT/JP99/03459	June 29,1999	⊠7 YES	□8 NO
			☐9 YES	□10 NO
			□11 YES	□12 NO
			□13 YES	□14 NO

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or PCT international application(s) designating the United States of American that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U.S.C. 120: STATUS (Check one) U.S. APPLICATIONS ABANDONED PATENTED PENDING U S. APPLICATION U.S FILING DATE NUMBER PCT APPLICATIONS DESIGNATING THE U.S. U.S SERIAL NUMBERS ASSIGNED PCT APPLICATION PCT FILING DATE (if any)



## COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

(Includes Reference to PCT International Applications)

POWER OF ATTORNEY:	As a named inventor, I hereby	appoint the following	attorney(s) with fu	Il power of
substitution and revocation,	to prosecute this application and	d transact all business	in the Patent and	<b>Frademark</b>
Office connected therewith.				

John M. DiMatteo (Reg. No. 32,690)

	l.	Correspondence		***		Direct Telephone (name and number)	Calls to: telephone
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\					John M. DiMatte (212) 336-2000	0	
		FULL NAME	FAMILY NAME	FIRST GIVEN NAME		SECOND GIVEN NAME	
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	2	RESIDENCE &	CITY	STATE OR FOREIGN CO	UNTRY	COUNTRY OF CITIZENS	SHIP
į	1	CITIZENSHIP	Saitama	JAPAN	JPX	Japanese	
			POST OFFICE ADDRESS	CITY		STATE & ZIP CODE/CO	UNTRY
į		POST OFFICE ADDRESS	2050-5, HARAGOU,	FUKAYA-SHI		Saitama JAPAN	366-0035
Г		2000	FAMILY NAME	FIRST GIVEN NAME		SECOND GIVEN NAME	
		OF INVENTOR	NAKAMOTO	Keizou			
i	2	RESIDENCE &	CITY	STATE OR FOREIGN CO	UNTRY	COUNTRY OF CITIZENS	SHIP
-	0 2	CITIZENSHIP _	Saitama	JAPAN []	PX_	Japanese	
		BOOT OFFICE	POST OFFICE ADDRESS	CITY		STATE & ZIP CODE/CO	UNTRY
i		POST OFFICE ADDRESS	c/o EISAI CO., LTD. 2-3-14, MINAMI,.	HONJYO-SHI		Saitama JAPAN	367-0048
		THE NAME	FAMILY NAME	FIRST GIVEN NAME		SECOND GIVEN NAME	
- 1		FULL NAME OF ANVENTOR	IIJIMA	Kazumi			·
	2	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN CO	UNTRY	COUNTRY OF CITIZENS	SHIP
	3		Gumma	JAPAN JP,	<u> </u>	Japanese	
-		POST OFFICE	POST OFFICE ADDRESS	CITY		STATE & ZIP CODE/CO	UNTRY
		ADDRESS	892-2, TSUNATORIMACHI,	ISESAKI-SHI		Gumma JAPAN	372-0812

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201	SIGNATURE OF INVENTOR 202	SIGNATURE OF INVENTOR 203
Kazuyuki Janase	Kelson Natamoto	Xolumi dillima
DATE	DATE	DATE
Dec 21, 2000	Dec 21. 2000	Dec 21.200

Additional inventors are being named on the attached sheet(s).

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